REMARKS

Applicants submit this amendment and response to the Examiner's Non-final Office Action dated March 31, 2010. The Office Action has been carefully reviewed and the following remarks are made in response thereto. Claim 54 is amended to recite "steroidal" aromatase inhibitors. Claims 58-60 are amended by changing their dependencies. Support for these amendments can be found throughout the specification. No new matter has been added.

Summary of the Office Action

1. Claims 54-71 are pending, with claims 70 and 71 being withdrawn from consideration.

2. Claim 56 was objected to for allegedly failing to further limit the claim from which it depends.

3. Claims 54 and 56-69 were rejected as allegedly lacking written description.

4. Claims 54 and 56-69 were rejected for allegedly failing to comply with the enablement requirement.

5. No claims were allowed. The Examiner had previously indicated in the Office Action dated July 6, 2009 that claim 69 was allowed and that claims 56, 57, 60, 64, and 65 were objected to as being dependent on a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Response to the Office Action

1. Claim objections under 37 C.F.R. §1.75(c)

Claim 56 was objected to for allegedly failing to further limit the subject matter of claim 54. The Examiner alleges that an aromatase inhibitor is an anti-estrogen. This objection is respectfully traversed.

Dependent claim 56 recites that the composition "further comprises" a therapeutically effective amount of an anti-estrogen, which clearly implies that the claimed "aromatase inhibitor" (claim 54) is distinct from the "anti-estrogen" (claim 56). *See, e.g., Clearstream Wastewater Systems, Inc. v. Hydro-Action, Inc.*, 206 F.3d 1440, 1446 (Fed. Cir. 2000) ("Under the doctrine of claim differentiation, it is presumed that different words used in different claims result in a difference in meaning and scope for each of the claims.").

Further, the specification makes an express distinction between these two substances. *See* page 8, lines 10-31. "[P]articularly ***two classes of substances*** ... are contemplated." Emphasis added. "On the one hand," anti-estrogens are those "substances which block estrogen receptors and therefore inhibit the effect of estrogen as antagonists." Aromatase inhibitors, by contrast, "may inhibit the extragonadal production of estrogens locally. To this end, steroidal and non-steroidal inhibitors of the (cytochromoe-p450)-aromatase are contemplated." The Examiner is reminded that "[A] patentee is free to be his own lexicographer." *Markman v. Westview Instrucments, Inc.*, 52 F.3d 967, 980 (Fed. Cir. 1995), aff'd, 517 U.S. 370 (1996).

Non-limiting examples of aromatase inhibitors are disclosed on page 9, line 1 to page 14, line 12. Non-limiting examples of anti estrogens are disclosed on page 14, lines 14-27.

The Examiner's assertion that claim 56 fails to further limit claim 54 is legally untenable under the doctrine of claim differentiation and also in light of applicant's definitions in the specification. Withdrawal of the rejection is respectfully requested.

2. Written Description – 35 U.S.C. §112, first paragraph (Office Action pages 2-3)

Claims 54 and 56-69 were rejected as allegedly lacking written description. Office Action at pages 2-3. The Examiner alleges that certain claim limitations which were added during prosecution, i.e., "identifying a subject suffering from a collagen deficient condition," and "to said subject in an amount sufficient to alleviate at least one symptom of said collagen deficient condition" are "new matter." According to the Examiner, the specification as-

filed (including the original claims) did not disclose these limitations. This rejection is respectfully traversed.

The Examiner identified two claim limitations that allegedly lack written description but gave absolutely no reasons why a person skilled in the art would not have recognized that the inventor was in possession of the invention as claimed. The rejection is inadequate under the USPTO's "Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, para. 1, 'Written Description' Requirement" at MPEP §2163. According to these guidelines, "[a] description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption." *Id.* "The examiner, therefore, must have a reasonable basis to challenge the adequacy of the written description. The examiner has the initial burden of presenting by a preponderance of evidence why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims." *Id.* "In rejecting a claim, the examiner must set forth express findings of fact regarding the above analysis which support the lack of written description conclusion." The Examiner made no attempt to "[e]stablish a *prima facie* case by providing reasons why a person skilled in the art at the time the application was filed would not have recognized that the inventor was in possession of the invention as claimed in view of the disclosure of the application as filed." *Id.*

An *en banc* Federal Circuit recently reiterated the well-known proposition that the written description requirement is not an *in haec verba* requirement. *Ariad Pharmaceuticals, Inc. v. Eli Lilly and Co.*, -- F.3d ----, 2010 WL 1007369, 13 (Fed. Cir. 2010) (*en banc*). In other words, new and amended claims do not have to use the exact words which were disclosed in the original specification. *See also* MPEP §2163 I.B. To the contrary, newly added claim limitations (in new or amended claims) may be supported in the specification through express, implicit, or even inherent disclosure. *Id.* The Federal Circuit has also stated "the applicant does not have to utilize any particular form of disclosure to describe the subject matter claimed, but the description must clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *Carnegie Mellon University v. Hoffmann-La Roche Inc.*, 541 F.3d 1115, 1122 (Fed. Cir. 2008).

Sufficiency of written description is assessed from the vantage point of the person having ordinary skill in the art. "Whether the written description requirement is satisfied is a fact-based inquiry that will depend on the nature of the claimed invention and the knowledge of one skilled in the art at the time an invention is made and a patent application is filed." *Id.* (internal citation omitted). According to the MPEP, in the context of new or amended claims, as is the case in the instant application, "[t]he fundamental factual inquiry is whether the specification conveys with reasonable clarity to those skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed." MPEP §2163 I.B.

The original specification unquestionably conveys to those skilled in the art that applicant was in possession of the instant claims at the time the application was filed. The original specification is replete with express references to collagen deficiencies and treatments that increase collagen content. For example, page 7, lines 4-11 discloses: "It was surprisingly found that said substance(s) or the composition containing this (these) substance(s) exhibit as a consequence of their action a positive influence on the collagen, particularly on the content of the collagen fibres within the collagen containing body region such as the skin, thereby rendering these body region more tight or firm. By means of biopsies it was found that the proportion of collagen fibres increased." Page 21, lines 13-20 discloses that a "characteristic of the skin of pregnancy strias is a decrease of collagen content." Page 22, line 34 – page 23, line 12 is directed to treatment of "collagen deficiency conditions," and discloses that according to the present invention, "the content of collagen fibres of the skin is increased." Page 23, lines 14-20 is directed to treating wrinkles in the face and open-necked regions, pregnancy strias or stretched strias at the lower abdomen, the thighs and the buttock and expressly discloses "to increase the percentage of collagen fibers of the skin." Page 24, lines 28-33 discloses "an increase of collagen fibers ... and accordingly to an increase of the thickness and tightness of the skin." Page 32, lines 29-30 discloses "sun-bathing decreases the collagen content of the skin."

Moreover, the examples and accompanying figures disclose actual reduction to practice of the claimed invention. "[P]ossession may be shown by describing an actual reduction to practice of the claimed invention." MPEP §2163 I.B. Although the examples do not use the exact phrase "identifying a subject suffering from a collagen deficient condition," the disclosure implies this step to a person having ordinary skill in the art. Moreover, the specification

expressly discloses that wrinkles and strias are "well visible especially in the case of dark skin color." Page 23, lines 19-20. Examples 1.1 and 1.2 are directed to a 60-year-old man and a 50-year old woman having "strong wrinkle formation[s]" in their eye regions. It is implicit from this disclosure that these subjects were "identified" for treatment because of these strong wrinkle formations. Similarly, example 2 discloses a subject having "strong formation of wrinkles in the lower region of the face, especially in the region of the cheek and chin." Example 3 discloses a woman with "wrinkles in the outer skin layer of the upper arms." Example 4.1 discloses a mother of two children having "strong pregnancy strias in the region of the abdomen." Example 4.2 discloses a woman having "stretched strias in the region of the thighs and buttock." It is implicit that the subjects in all of the disclosed examples were "identified" and that they were "suffering from a collagen deficient condition." Moreover, page 22 line 34 of the original specification discloses "treating collagen deficiency conditions of the outer skin." (emphasis added). Accordingly, the original specification unquestionably conveys to a person having ordinary skill that applicant was in possession of the clamed invention.

The examples also do not use the exact phrase "to said subject in an amount sufficient to alleviate at least one symptom of said collagen deficient condition." However, this limitation is also implicit to a person having ordinary skill in the art. Example 1.1 discloses a ten week treatment resulting in "an almost disappearance of the wrinkles." Example 1.2 discloses an eight week treatment resulting in "strong smoothening of the upper skin in the region of the wrinkle formation around the yes" and after sixteen weeks the "wrinkles have disappeared. Example 2 discloses a six week treatment resulting in noticeable smoothing of wrinkles and a twelve week treatment resulting in only slight visible wrinkles. Examples 3 discloses a successful 16 week treatment resulting in the wrinkles becoming "practically invisible." Figures 1 and 2 discloses biopsies before and after this treatment. Example 4.1 discloses a treatment eliminating pregnancy strias. Example 4.2 discloses a successful treatment, making the strias become "practically not visible." Figures 3 and 4 show the subject before and after this treatment. Accordingly, the original specification unquestionably conveys to a person having ordinary skill that applicant was in possession of the clamed invention. It is implicit in each of these disclosures that the symptoms were "alleviated."

Withdrawal of the rejection is respectfully requested.

3. Written Description – 35 U.S.C. §112, first paragraph (Office Action page 11)

Claims 54, 59, 60, and 62-64 were rejected as allegedly failing to comply with the written description requirement. Office Action at page 11. This rejection is respectfully traversed.

Claims 58-60 are amended by changing their dependencies. Claim 58 now depends from claim 56, claim 59 now depends from claim 57, and claim 60 now depends from claim 57. Claim 54 is amended to recite "steroidal" aromatase inhibitors. No new matter has been added.

The claims, as amended, are directed to a cosmetic treatment by topical administration of one of three genus of compositions comprising effective amounts of:

- Genus 1: a **steroidal aromatase inhibitor** (claims 54, 51-69);
- Genus 2: a **steroidal aromatase inhibitor** ***and*** an **anti-estrogen** (claims 56 and 58);
- Genus 3: a **steroidal aromatase inhibitor** ***and*** a **5-alpha-reductase inhibitor** (claims 57 and 59-60).

These amendments to the dependencies accommodate the Examiner's concern that the specification allegedly lacks written description for components that have "dual abilities." *See e.g.*, Office Action at page 14 last paragraph, page 15 ("the specification does not disclose the relationship between the structure of an inhibitor that has the **dual ability** to inhibit aromatase **and** 5-alpha-reductase **or** the production and/or effect of dihydrotestosterone.") (emphasis added). *See also* Office Action page 16, last paragraph to page 17 first paragraph. These amendments clarify that the aromatase inhibitor, which may be sterol isolated from soya glycines (Genus 1: claim 63 and 64), is **not** the component which locally inhibits the production and/or effect of estrogens (Genus 2: claim 58), and is **not** the component which locally inhibits the production and/or the effect of dihydrotestosterone (Genus 3: claim 59) or locally inhibits aromatase activity and 5-alpha-reductase activity (Genus 3: claim 60).

The specification has adequate written description for each of the three claimed genus. Regarding **Genus 1, steroidal** aromatase inhibitors, the specification discloses on page 8, lines 33-34 "Examples of aromatase inhibitors include the following substances" and pages 9-11 disclose dozens of steroidal aromatase inhibitors, while pages 11-12 disclose dozens of non-steroidal aromatase inhibitors. Page 12 discloses "other" aromatase inhibitors. Page 13 discloses various references which further disclose aromatase inhibitors.

Methods of making these inhibitors are well-known in the art; what is well-known need not be disclosed and is best omitted. *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991). In particular, methods of making ***steroidal*** aromatase inhibitors, for example Formestane, are well-known in the art. Pages 13-14 specifically discloses making soya derived aromatase inhibitors "by means of topical separation methods, such as liquid chromatography, particularly by means of HPLC." Oxidation of soya glycines is described. "The oxidation can be carried out by an enzymatic approach, for example according to the method described by Y. Fujimoto et al. ... or by a chemical approach, for example according to the method described by P. Welzel..." Moreover, the examples disclose actual reduction to practice of oxidized soya glycines (examples 1-4) and the steroidal aromatase inhibitor Formestan (example 5). Further, methods of making soya glycines, including oxidation of soya glycines, were known in the art. *See, for example*, U.S. Patent No. 5,945,109.

The additional component in **Genus 2**, anti estrogens, have written description on page 14, lines 14-23. As stated above with regards to the objection under 37 C.F.R. 1.75(c), the "anti estrogen" component is a distinct component from the "aromatase inhibitor" component in Genus 2. Methods of making anti estrogens are well-known in the art; what is well-known need not be disclosed and is best omitted. *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991).

The additional component in **Genus 3**, 5-alpha-reductase inhibitors, have written description on pages 15-17. Methods of making 5-alpha-reductase inhibitors are well-known in the art; what is well-known need not be disclosed and is best omitted. *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991).

According to the Office's written description guidelines, written description for a claimed genus can be shown by either a reduction to practice of a "representative number" of a species, **or** by disclosure of relevant identifying characteristics e.g., structure, physical/chemical properties, or functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such characteristics. MPEP §2163. Here, the specification not only discloses various ***steroidal*** aromatase inhibitors, it shows reduction to practice of two species (soya glycines and Formestan). Therefore, the specification has written description and enablement for *at least* these two species. Written description can be satisfied even without a reduction to practice of a representative number of species when the specification discloses relevant identifying characteristics or functional characteristics coupled with a known correlation between function and structure. In this case, steroidal aromatase inhibitors share a common sterane core. Moroever, unlike the non-steroidal aromatase inhibitors, the steroidal aromatase inhibitors are able to effectively penetrate the dermis in order to reach the underlying collagen. In this case, the specification provides written description for steroidal aromatase inhibitors because they share a common core and two such species are shown reduced to practice.

4. Enablement – 35 U.S.C. §112, first paragraph (Office Action at page 3)

Claims 54 and 56-69 were rejected as allegedly failing to comply with the enablement requirement. This rejection is respectfully traversed.

The initial burden is on the Examiner to establish a reasonable basis to question the enablement provided in the disclosure. MPEP §2164.04. The Examiner appears to doubt that the disclosed examples of wrinkles and stryias treated with oxidized soya glycines works as claimed; *See* Office Action at pages 7-8. This type of rejection is improper. "[I]t is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure." *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). Methods of making the claimed **steroidal** aromatase inhibitors

are discussed above in reference to the written description requirement; those arguments are incorporated here.

The Examiner admits that the skill in the art is high, generally that of a medical doctor or Ph.D. biochemist. Office Action at page 5. Administration of the claimed substances is not particularly difficult to a person having ordinary skill in the art. As such, the claimed invention can be practiced with routine experimentation. Further, as discussed above, the specification gives ample written description to making steroidal aromatase inhibitors, anti-estorgens, and 5-alpha-reductase inhibitors; indeed, many of these substances are well-known to one of ordinary skill. Also as discussed above—despite the Examiner's contrary allegations—the specification also enables oxidation of soya glycines as well as disclosing actual reduction to practice. Moreover, the Examiner failed to recognize that methods of making soya glycines, including oxidation of soya glycines, were already known in the art. *See, for example*, U.S. Patent No. 5,945,109. Formestane, another steroidal aromatase inhibitor reduced to practice at example 5, is also readily made by techniques known in the art. Quantity of examples is only one factor that must be considered before reaching the final conclusion that undue experimentation would be required. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404.

According to the MPEP, if a rejection is made based on the view that enablement is allegedly not commensurate in scope with the claim, the Examiner should at least identify the subject matter is considered to be enabled. MPEP §2164.08. As shown above, the specification provides a detailed listing of inhibitors, all of which can be made using prior art techniques. Further, the examples provide actual reduction to practice of the steroidal soya glycines and Formestan. As long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112 is satisfied. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). In this case, steroidal aromatase inhibitors share a common sterane core. Moroever, unlike the non-steroidal aromatase inhibitors, the steroidal aromatase inhibitors are able to effectively penetrate the dermis in order to reach the underlying collagen.

Failure to disclose other methods by which the claimed invention may be made does not render a claim invalid under 35 U.S.C. 112. *Spectra-Physics, Inc. v. Coherent, Inc.*, 827

F.2d 1524, 1533, 3 USPQ2d 1737, 1743 (Fed. Cir.), *cert. denied*, 484 U.S. 954 (1987). Not everything necessary to practice the invention need be disclosed. In fact, what is well-known is best omitted. *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991). All that is necessary is that one skilled in the art be able to practice the claimed invention, given the level of knowledge and skill in the art. If a statement of utility in the specification contains within it a connotation of how to use, and/or the art recognizes that standard modes of administration are known and contemplated, 35 U.S.C. 112 is satisfied. *In re Johnson*, 282 F.2d 370, 373, 127 USPQ 216, 219 (CCPA 1960); *In re Hitchings*, 342 F.2d 80, 87, 144 USPQ 637, 643 (CCPA 1965). For example, it is not necessary to specify the dosage or method of use if it is known to one skilled in the art that such information could be obtained without undue experimentation. If one skilled in the art, based on knowledge of compounds having similar physiological or biological activity, would be able to discern an appropriate dosage or method of use without undue experimentation, this would be sufficient to satisfy 35 U.S.C. 112, first paragraph. MPEP §2164.01(c).

CONCLUSION

Applicant believes that the above-reference application is in condition for allowance. Reconsideration and withdrawal of the outstanding rejections and objections and early notice of allowance to that effect is respectfully requested.

EXCEPT for issue fees payable under 37 C.F.R. § 1.18, the Director is hereby authorized by this paper to charge any additional fees during the entire pendency of this application, including fees due under 37 C.F.R. §§ 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account No. 13-3250, reference No. 38891.00100US. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F. R. § 1.136(a)(3).

Respectfully submitted,

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